

RESEARCH

FALL 2018

Matters



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DOING WHAT'S BEST.®

McLAREN NEUROSURGEON MAKES HEADLINES IN FOUR MAJOR ACADEMIC PUBLICATIONS IN JULY 2018

Sunil Manjila MD., neurosurgeon at McLaren Bay Region, is making headlines in the world of academic research by having four original articles published in three prestigious neurosurgical journals, including two that made the cover pages of these journals, all in the month of July 2018.

His articles were featured in three Pubmed-indexed neurosurgical journals, including *Neurosurgery*, *Journal of Neurosurgery* and *Neurosurgical Focus* for the month of July 2018, links to which are found at www.Pubmed.gov. The articles are titled:

- “A Morphometric Survey of the Parasellar Region in more than 2700 Skulls: Emphasis on the Middle Clinoid Process Variants and Implications in Endoscopic and Microsurgical Approaches.” *Journal of Neurosurgery*. 2018 Jul;129(1):60-70.
- “Intratympanic Rathke’s Cleft Cyst Remnants Within Craniopharyngioma, Pituitary Adenoma, Suprasellar Dermoid, and Epidermoid Cysts: A Ubiquitous Signature of Ectodermal Lineage or a Transitional Entity?” *Neurosurgery*. 2018 Jul 12. doi: 10.1093/neuros/nyy285
- “Jugular Bulb and Skull Base Pathologies: Proposal for a Novel Classification System for Jugular Bulb Positions and Microsurgical Implications. *Neurosurgical Focus*. 2018 Jul;45(1):E5.
- “A Review of Extraaxial Developmental Venous Anomalies of the Brain Involving Dural Venous Flow or Sinuses: Persistent Embryonic Sinuses, Sinus Pericranii, Venous Varices or Aneurysmal Malformations, and Enlarged Emissary Veins.” *Neurosurgical Focus*. 2018 Jul;45(1):E9.

The last two of these papers published by Dr. Manjila featured two original classifications: Manjila and Semaan classification of jugular bulb positions and Manjila grading for persistent falcine sinuses, the former was archived for posterity by the Journal of Neurosurgery Publishing group and podcasted, truly a personal and academic milestone for this scholarly neurosurgeon. As a testimony to his academic achievements, Dr. Manjila’s papers were cited well over 1000 times since 2009 to date according to Google Scholar (h-index 13 and i10 index 34). Dr. Manjila is a passionate researcher who has made significant contributions in neurosurgical research in over 90 Pubmed-indexed publications. He enjoys sharing his neurosurgical knowledge and skill in performing neurosurgical procedures with medical students and residents who rotate with him on the neurosurgical service line. As a Clinical assistant professor in neurology, he also does innovative and collaborative research in skull base and robotics, while serving as institutional Principal Investigator for VIGILANT trial (neuro-oncology) and having a patent pending for an epoch-marking “MRI-compatible cranial neuro-endoscope”.

The neurosurgical procedures Dr. Manjila performs include: skull base surgery and microsurgical aneurysm treatment, transcranial endoscopy and pituitary surgeries, intracranial tumors and awake craniotomy, complex spine surgery as well as pain-stimulators and pumps. Dr. Manjila notes that, “Innovation and research can offer huge incentives for progress in neurosurgical practice, providing a thrust for technical improvement in my own domain of surgical work”.



Dr. Sunil Manjila and his operating room crew.



Dr. Manjila with clinical trial staff Kelly Kayner (right) and Linda Jaskiewicz (left) working on VIGILANT Trial.

RESEARCH AROUND McLAREN

Currently over 130 active research studies and projects are being conducted by clinical investigators and their research teams throughout McLaren Health Care and its subsidiaries. This number includes both non-oncology and oncology studies. We would like to highlight some of the cutting edge innovative research projects being conducted here at McLaren.

McLaren Macomb and **McLaren Flint** research teams were recognized as one of the top 4 enrolling sites across the United States in the **TARGET New Nano Registry**. The purpose of this prospective registry is to collect real world, post-marketing data on the use of Stryker Target® 360, Target® 2D, Target® Helical and 2nd generation Target® Nano coils for the embolization of ruptured or unruptured intracranial saccular aneurysms.

Congratulations to the TARGET research team: Primary Investigator Aniel Majjhoo, MD, Co-Investigator Bharath Naravetla, MD, and Clinical Research Associates Valentyna Onishchuk, Bernice Edwin, and Melissa Szemites!

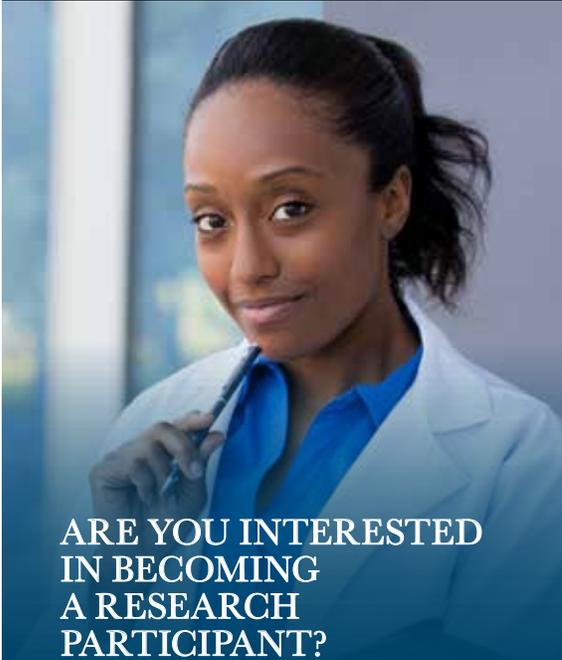
McLaren Macomb and **McLaren Northern** tied for 1st place in the Midwest region in the **CONNECT-HF** study summer enrollment challenge. The purpose of this trial is to evaluate the effect of a customized, multifaceted, health system-level quality improvement (QI) program compared with usual care on heart failure (HF) outcomes and HF quality-of-care metrics.

Congratulations to the Macomb CONNECT-HF research team, Primary Investigator Timothy Logan, DO, Co-Investigator Melissa Iantelli, DO and Clinical Research Associates Valentyna Onishchuk and Bernice Edwin. Macomb Northern CONNECT-HF research team, Primary Investigator Gerald Gadowski DO, Clinical Research Associates Denise Antonishen, Colleen Shaw, and Peggy Ward.

McLaren Northern's Dr. Colfer was spotlighted for reaching a significant enrollment milestone of 15 subjects in the **CLEAR Outcomes** study. The primary objective of this study is to evaluate whether long-term treatment with bempedoic acid 180 mg/day versus placebo reduces the risk of Major Adverse Cardiovascular Events (MACE) in patients with, or at high risk for, cardiovascular disease (CVD) who are statin intolerant. The sponsors expressed appreciation for McLaren Northern's commitment and continued efforts, specifically their efforts to minimize missing data by ensuring the continued participation of all randomized patients. One of the biggest challenges in clinical trials is the ability to retain patients and minimize missing data.

Congratulations to the Northern CLEAR research team, Primary Investigator Dr. Harry Colfer MD, Co-Investigator Gerald Gadowski, DO and Clinical Research Associates Denise Antonishen, Colleen Shaw and Peggy Ward.

If you want your research study featured in an upcoming newsletter, contact Patricia Ivery, Corporate Research Manager at patricia.ivery@McLaren.org.



ARE YOU INTERESTED IN BECOMING A RESEARCH PARTICIPANT?

For information on enrolling in a clinical trial please visit our website at <https://www.mclaren.org/main/research-trials1.aspx>. Here you will find a list of open enrolling studies at McLaren, including which hospital the research is being done at and contact information for each study.

We have enrolling studies for the following conditions (not a complete list):

- Diabetes
- High Blood Pressure (Hypertension)
- Stroke
- Heart Attacks / Heart Failure / Heart Disease
- Kidney Diseases
- Lung Diseases
- Peripheral Artery Disease
- Carotid Artery Disease
- Mastectomy
- Various Cancers
 - Breast
 - Lung
 - Prostate
 - Multiple Myeloma
- Patients who underwent intracranial aneurysm coiling
- Drug study for patients with recent acute coronary syndrome

For a complete list of conditions, please visit our website listed above.

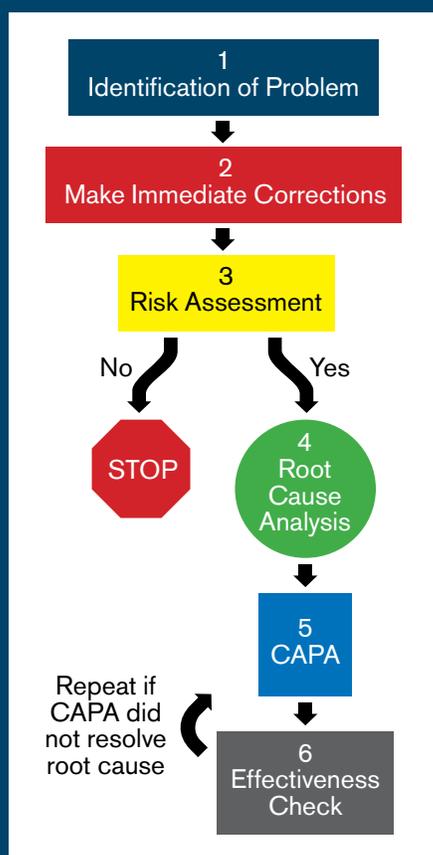
EQUIP CORNER

MOVING FORWARD WHEN THE UNEXPECTED HAPPENS PART 2

By Patricia Ivery

Figure 1.

SYSTEMATIC APPROACH



In our last newsletter we left off at determining the root cause of deviations that require a corrective action preventative action (CAPA) plan. In this issue, we will discuss creating corrective and preventative actions to eliminate the root cause. Well documented and executed CAPA plans are an underlying expectation from the Food and Drug Administration (FDA), Office of Human Research Protection (OHRP) and the Institutional Review Board (IRB). In addition, CAPA plans are addressed in the ICH document on good clinical practice guidelines (GCP).

We never know when an external regulatory agency is going to knock on our door announcing an audit of clinical research records. Hopefully, researchers have discovered their significant deviations and instituted a CAPA plan beforehand. It is better to plan a strong offense rather than scramble for defense. A good CAPA plan can be the difference between a study remaining open or being involuntarily closed.

The FDA has made it very clear, both in public presentations and warning letters to sponsors and clinical investigators, that they expect when good non-compliance occurs there is: (1) an investigation regarding how widespread the problem is and (2) description of efforts into the prevention of the problem in the future. If an FDA observation form 483 is issued after an audit, the site should respond with a CAPA plan. Although there is no regulatory requirement for the inspected party to respond with a CAPA plan, doing so may mitigate further actions by the FDA. Furthermore, initiation of a CAPA plan demonstrates commitment and intent to comply which will establish credibility with the FDA. A heed of warning though, when the inspected party chooses to provide a written CAPA in response to a warning letter, the thoroughness of the CAPA plan will be addressed. Common deficiencies noted in warning letters regarding CAPA plans include:

- insufficient detail or inadequate documentation on the specific corrective actions to be taken
- not describing the extent of the problem
- not describing the preventative measures to be taken
- not describing the extent/pervasiveness of the problem
- not providing the timeframe in which corrective actions have been or will be undertaken/completed

OHRP, in their assessment of research incident reports, looks closely at the adequacy of the actions taken by the institution to address the problem. Specifically, whether the corrective actions will help ensure that the incident will not be repeated, either with the investigator or protocol in question, or with any another investigator or protocol at the institution. Therefore, OHRP recommends corrective actions be applied “institution-wide”, when appropriate, not just with the investigator in question.

Here at MHC, investigators must follow MHC policy MHC_PR0122 on protocol deviations and violations. This policy states that significant protocol violations must be submitted to the MHC IRB via eProtocol within two business days of the study team’s knowledge of the event. The eProtocol violation submission form requires a description of corrective and preventative actions.

The revised changes to the ICH Guidelines on Good Clinical Practice Guidelines (E6 R2) addendum calls on sponsors and investigators to implement additional quality assurance safeguards, specifically a risk assessment process covering trial conduct. GCP principles section 5.20.1 states that if non-compliance affects

or has the potential to significantly affect human subject protection, or if reliability of trial results is discovered, the sponsor should perform a root cause analysis and implement appropriate corrective and preventative actions.

Documenting the CAPA plan for significant deviations is vital. If the CAPA plan is not thoroughly documented, auditors and regulators will assume it was not done and that the investigator did not consider significant deviations a serious matter. When writing, executing and evaluating effectiveness of a CAPA plan include the following:

1. State the problem to describe the specifics of the inspection findings while also addressing potential system-wide or global implications including the root cause.
2. Include both corrective and preventative actions in the CAPA. Corrective actions are immediate or reactive actions to correct/eliminate an issue that has already occurred or has been identified. Preventative actions are proactive actions to prevent the cause and problem from happening again. Preventative actions often involve development of new procedures or processes. One of the most common features of a CAPA plan is additional education and training.
3. Create action statements using the SMART acronym system:
 - S** stands for **Specific**. The action statement should indicate compliance with regulations and full observation of the root cause.
 - M** stands for **Measurable**. The action should be able to be measured to demonstrate whether it is adequate to address root cause.
 - A** stand for the **Action** being achievable.
 - R** stands for **Realistic**. Ask yourself, can thee plan can be carried out given the current resources, knowledge and expertise.
 - T** for **Time bound**. The action should indicate a target date for completion addressing critical or urgent deviations appropriately. Reflect the outcome of the root cause analysis and include, where appropriate, plans to achieve immediate, short and long-term corrections within stated timeframes.
4. Identify the person or persons accountable for each action.
5. Identify the necessary resources to support the actions such as staffing, funding, education, training, etc.
6. Train all applicable staff on the CAPA plan, ensuring copies of plan have been distributed to the necessary parties.
7. The CAPA plan must include copies of any supporting documentation that is referenced. For example, teaching plan, training log, procedure checklists, etc.
8. A good CAPA plan should have a built-in effectiveness checking mechanism to verify and validate that the CAPA system is working. Document and execute a way to verify and/or monitor the effectiveness of the planned corrective actions. For example, scheduled future self-audit.
9. Once the plan is implemented investigators should keep records describing when and how each element of the plan was achieved.
10. Maintain transparency of the CAPA plan. Besides documentation, communication is key to a successful CAPA plan. Investigators and their team should not only discuss the CAPA plan, but its outcome after implementation. File the CAPA plan and effectiveness checking documentation. Don't forget to share the plan with sponsors, IRB, administrations, and/or external agencies as required.

Remember, it is better to plan a strong offense rather than defense. If you need assistance in developing a CAPA plan contact the Office of Research Compliance and QI.

UPCOMING RESEARCH EDUCATION

SOCRA 27th Annual Conference
New Orleans, LA
Sept 28-30, 2018

**MAGI Clinical Research
West Coast Conference**
San Diego, CA
Oct 21-24, 2018

PRIM&R
San Diego, CA
November 14-17, 2018

ACRP
Nashville, Tennessee
April 12-15, 2019

RESIDENT CORNER

QUALITY IMPROVEMENT PROPOSALS

By Carlos F. Rios-Bedoya, ScD, Corporate Director of Scholarly Inquiry

Quality Improvement (QI) projects are one way to meet the Accreditation Council for Graduate Medical Education (ACGME) residency requirements for scholarly activity. Prior to beginning a QI project, residents need to have their project approved by the Scholarly Activity Review Committee (SARC). Residents initiate this process by filling out the required forms, which can be found on the New Innovations webpage of each subsidiary or by requesting them from the Director of Medical Education (DME) at your subsidiary. It is highly recommended that residents' QI projects be aligned with their hospital's QI priorities. Once all required documents are complete, email the forms and any supporting documents to sarc@mclarenmeded.org. Please CC Dr. Carlos Rios-Bedoya at carlos.rios@mclaren.org on each submission as well.



Carlos F. Rios-Bedoya, ScD

For SARC to move forward with the review of a QI proposal, all required forms must be filled out completely. Incomplete forms, including forms without signatures, delay the review process because they are returned to the principal investigator (PI) for completion and resubmission. One area that seems challenging is Section H of the SARC New Application Form (Figure 1 shown below). This is one of the most important sections of the application form. This is where the investigator explains all the aspects and steps needed to successfully complete the QI project. A clear and concise narrative description of the QI proposal should be included in this section. SARC reviewers will use this information to evaluate the QI proposal and provide feedback to the PI.

Instructions on how to fill out Section H can be found in the document QI Proposal Guidelines v2, also located on the New Innovations website. It is always important to follow any instructions provided. If you have any questions regarding any of the forms or the QI project submission process, contact your DME, program director, faculty mentor, or the Corporate Director of Scholarly Inquiry.

Best of luck with your QI projects.



RECOGNIZING MCLAREN RESIDENTS

McLaren Flint residents presented at the 2018 Southeast Michigan Center for Medical Education Research Forum. This forum's purpose is to “recognize outstanding research by residents and highlight the importance of research as a component of the graduate medical education training experience”.

Angela Collins, MD, PhD won third place for her slide presentation: “Restraint Use and Injuries in Pregnant Women Involved in Motor Vehicle Crashes”.

Congratulation Dr. Collins!

FIGURE 1

SECTION H: NARRATIVE DESCRIPTION

Attach a concise narrative description of the scholarly activity project. Include the following elements (follow the QI Proposal Format Guidelines):

- A. Abstract
- B. Aims/objectives of the study
- C. Background/Motivation for doing the study
- D. Project Design and Procedures
- E. Time line, QI Status, Team, Future Plans, and Sustainability

WHAT'S NEW?

CTMS UPDATE

McLaren Center for Research and Innovation continues the process of implementing a Clinical Trials Management System (CTMS) to support research operations across the system. Our system, IBM CTMS for Sites, allows clinical research administration to streamline current workflows and manage study progress and finances.



McLaren Greater Lansing was the first site to roll out the CTMS. McLaren Bay Region is the next site that the CTMS for Sites system will be implemented, which is currently slated to go live in September 2018.

STAFF ACKNOWLEDGEMENTS

We would like to acknowledge and congratulate the following research staff for their professional achievements:

Bachelor of Science in Nursing

- Kelly Kayner RN, CRA obtained her BSN from Ohio University



Kelly Kayner

Certified Clinical Research Professional (CCRP®) through the Society of Clinical Research Associates (SOCRA).

This accomplishment recognizes continuing excellence in the ethical conduct of clinical trials. SOCRA's International Certification Program based on internationally-accepted standard of knowledge, education, and experience.

- Laura Powell RN, BS, CRA – McLaren Bay Region
- Katherine Ashworth, CRC II- Study Coordinator KCI
- Paige Dykema CRC II- Regulatory Coordinator KCI
- William Elliott, CRC II- Study Coordinator KCI
- DeQuindalyn Moore, CRC II- Study Coordinator KCI
- Nikita Patel, CRC II- Study Coordinator KCI
- Michelle Pomerleau, CRC II- Study Coordinato KCI
- Christopher Salas, CRC II- Study Coordinator KCI



Laura Powell



Katherine Ashworth



Paige Dykema



William Elliott



DeQuindalyn Moore



Nikita Patel



Michelle Pomerleau



Christopher Salas

NEW STAFF ANNOUNCEMENTS



Marybeth McCarthy

Marybeth McCarthy, QI & Education Specialist

Marybeth McCarthy, RN, BSN joins us as the new QI and Education Specialist in the Research Integrity department. Marybeth brings a wealth of experience with over 12 years in the field of clinical trials. As a RN has worked in inpatient medical-surgical units, intensive care, outpatient, case

management, home care, and pediatric and adult private practice offices. Most recently worked at Henry Ford Hospital in the Oncology department as a research coordinator. She has worked as a coordinator in other fields such as; infectious diseases, internal medicine, cardiology, and rheumatology. Marybeth also worked as a CRA for the contract research organization Covance.



Lindsey Packer

Lindsey Packer, Contract and Budget Specialist

MCRI is pleased to announce the appointment of Lindsey Packer to the position of Post-Award Contract and Budget Specialist. Lindsey brings with her extensive research experience from the Mayo Clinic in Minnesota, where she worked as a research coordinator and then as a program

coordinator. Here her research experience and responsibilities ranged from conducting and managing multi-site clinical trials, to grant writing, to managing research contracts, budgets as well as fund management. Most recently, she has been with McLaren at MMG, where she was the operations manager for three MMG clinics.



Mary Canton

Mary Canton, CRA McLaren Northern MI

MCRI would like to announce that Mary Canton, RN, BSN has joined our MCRI team at McLaren Northern Michigan as a Clinical Research Associate. Mary comes to us from Endoscopy at McLaren Northern Michigan, where she worked as an RN, Clinical Coordinator, and Team Leader. Mary has been with McLaren Northern Michigan since

1978 and in addition to her time spent with Endoscopy, she spent some time working in the Medical Surgery Unit. Mary is a member of the Karmanos Cancer Institute McLaren Northern Michigan Cancer Committee and has previously served as a MAGNET council unit representative, Nursing Clinical Ladder Council Chair, co-chair of Michigan Society of Gastroenterology Nurses

and Associates, and was also a member of Northern Michigan Hospital's Nurse Executive Committee.



Sri Yarlagadda

Sri Vidya Yarlagadda, Regulatory Specialist

MCRI welcomes Sri Vidya Yarlagadda to our regulatory team. Vidya has 15+ years of clinical research experience, particularly in oncology research. She has worked across various facets of clinical trials arena including drug design, development and manufacturing, drug testing in phase I/II

clinical trials, as well as in regulatory management of clinical trials. She has extensive research experience in developing and testing targeted immunotherapy treatments for cancer. Additionally, she has done study coordination and regulatory management of oncology trials and has extensive experience initiating investigator-initiated trials, submitting Investigational New Drug (IND) applications, and managing all FDA related regulatory tasks for INDs. Vidya comes to us from KCI, where she previously worked in the regulatory department of the clinical trials office.



Sydney Whitson

Sydney Whitson CRC 1 KCI Lansing

We would like to welcome Sydney Whitson, BS, Clinical Research Coordinator I. Sydney joined our Karmanos Cancer Institute Clinical Trials Office team on May 21, 2018 to support the Oncology research program at Karmanos Cancer Institute at McLaren Greater Lansing and Mid-Michigan Physicians. Sydney earned her Bachelor of

Science degree in Biomedical Science from Western Michigan University and has worked as a Medical Scribe as well as a Patient Care Associate.



Tallat Mahmood, MD

New IRB Member

A warm welcome is extended to **Dr. Tallat Mahmood** as our newest member of the MHC IRB. Dr. Mahmood is a board certified Internal Medicine and Hematology/Oncologist at Karmanos Cancer Institute (McLaren Greater Lansing). She joined McLaren's IRB effective June 1, 2018. Dr. Mahmood attended medical school at AGA

Khan University Medical College, completed her Internal Medicine residency at West Virginia University, and her Hematology/Oncology fellowship at Tulane University of Louisiana School of Medicine. Welcome to the Board, Dr. Mahmood!

McLaren Corporate Research

2701 Cambridge Court, Ste. 110
Auburn Hills, MI 48326

Office of Clinical Excellence

VICE PRESIDENT

Chandan Gupte
chandan.gupte@mclaren.org

Corporate Research Administration

RESEARCH ADMINISTRATOR COORDINATOR

Markeda Richards
markeda.richards@mclaren.org

ADMINISTRATIVE ASSISTANT

Tamara Leo
tamara.leo@mclaren.org

Research Integrity

hrpp@mclaren.org
(248) 484-4950

IRB ANALYSTS

Katherine Pittel
katherine.pittel@mclaren.org

QI & EDUCATION SPECIALIST

Marybeth McCarthy
marybeth.mccarthy@mclaren.org

McLaren Center for Research and Innovation

mclaren.org/Main/Research.aspx
(248) 484-4960

CORPORATE RESEARCH MANAGERS

Jill George
jill.george@mclaren.org

Patricia Ivery
patricia.ivery@mclaren.org

REGULATORY SPECIALIST

Tanya Gardner-Mosley
tanya.gardner-mosley@mclaren.org

Vidya Yarlagadda
yarlagas@karmanos.org

CONTRACT & BUDGET SPECIALISTS

Linsey Packer
linsey.packer@mclaren.org

Stephanie Edwards
stephanie.edwards@mclaren.org

Karmanos Cancer Institute Clinical Trials Office

VICE PRESIDENT

Lisa Lange
langel@karmanos.org

DIRECTOR

Maureen Kelley
kelley@karmanos.org

MANAGER

Elizabeth Bowie
bowie@karmanos.org